Rejection Under 35 U.S.C. § 103(a)

The Examiner has maintained the rejection of claims 1, 5, 7-10, 12-18, and 20-26 under 35 U.S.C. § 103(a) as unpatentable over Liao, et al., (U.S. Patent No. 6,147,109) in view of Niewohner, et al., (WO 99/24433); claims 6 and 19 under 35 U.S.C. § 103(a) as unpatentable over Liao, et al., (U.S. Patent No. 6,147,109) in view of Niewohner, et al., (WO 99/24433) and in further view of Doherty, et al., (U.S. Patent No. 6,037,346); claims 1, 5, 7-10, 12-18, and 20-26 under 35 U.S.C. § 103(a) as unpatentable over Liao, et al., (U.S. Patent No. 6,147,109) in view of R&D Drug Review (1998); and claims 6 and 19 under 35 U.S.C. § 103(a) as unpatentable over Liao, et al., (U.S. Patent No. 6,147,109) in view of R&D Drug Review (1998) and in further view of Doherty, et al., (U.S. Patent No. 6,037,346) (Paper No. 05062004, pages 2- 6). Applicants respectfully traverse.

The Examiner cites Liao, et al., (U.S. Patent No. 6,147,109) as the primary prior art over the claimed invention. Liao, et al., discloses the use of HMG-CoA reductase inhibitors to treat a myriad of conditions including, for example, pulmonary hypertension, stroke, heart failure, hypoxia-induced conditions, insulin deficiency, impotence, renal disease, gastric motility syndrome, atherosclerosis, transplant arterial sclerosis, arthritis, lupus, scleroderma, emphysema, etc. (*see, e.g.,* column 7, lines 34-52). Specifically, Liao, et al., discloses that HMG-CoA reductase inhibitors up-regulate endothelial cell nitric oxide synthase. As one skilled in the art would appreciate, the diseases disclosed by Liao, et al., may result from any number of etiologies. Thus, it is speculative that one drug class, that is, an inhibitor of HMG-CoA reductase would be successful in treating these diverse disease conditions.

In addition, Liao, et al., discloses an extensive list of "second agents" (>100 agents) that may be co-administered (column 13, line 14 to column 14, line 17). However, these second agents are very broad classes of pharmaceutical agents such as antagonist, cardiovascular agent, hormone, etc., and each individual class of agents represents a large number of compounds. For example, an antagonist could encompass any compound that possesses antagonistic activity which may represent thousands of compounds. Likewise, an impotence therapy adjunct would also encompass a large number of agents. For that matter, the class of drugs known as HMG-CoA reductase inhibitors also represents a large number of compounds. It would reasonable to estimate that the disclosure of Liao, et al., represents thousands of possibilities, and there is no suggestion whatsoever as to which of these many possibilities would be successful. Indeed, based on the disclosure by Liao, et al., it would reasonable to state that it would require undue experimentation by one skilled in the art to identify the specific HMG-CoA reductase inhibitor and the specific second agent that would effective in treating one of the many diseases disclosed.

In fact, the disclosure by Liao, et al., actually represents an "obvious-to-try" situation. That is, this general disclosure does not contain a sufficient teaching of how to obtain the claimed invention. The

prior art provides no indication of which parameters are critical (e.g., dosage) or no direction as to which of the many possible choices is likely to be successful. As discussed above, Liao, et al., disclose numerous disease indications, numerous HMG-CoA reductase inhibitors, and numerous second agents, but one skilled in the art would have no idea which disease indication and which combination of HMG-CoA reductase inhibitors and second agents would actually be successful. Moreover, there is no guidance as to effective dosages, treatment schedules, etc.

"Obvious-to-try" is not the standard under 35 U.S.C. § 103 (In re O'Farrell, 853 F.2d 894). A claimed invention is obvious-to-try if the prior art gives "only general guidance as to the particular form of the claimed invention or how to achieve it" (In re O'Farrell, 853 F.2d 894, 903). Furthermore, "whether a particular combination might be obvious-to-try is not a legitimate test of patentability" (In re Fine, 837 F.2d 1071, 1075). As discussed above, the disclosure of Liao, et al., provides little guidance as to which combination would likely to be successful. Thus, the combination of the claimed invention may be obvious-to-try based on Liao, et al., but certainly not obvious.

Furthermore, to support an obviousness rejection, the prior art must not only suggest the claimed composition, but also, one of ordinary skill in the art must have a reasonable expectation of success.

Based on the disclosure of Liao, et al., there is no reasonable expectation that of all the possible combinations disclosed that the combination of the claimed invention, 2-[2-ethoxy-5-(4-ethyl-piperazine-1-sulfonyl)-phenyl]-5-methyl-7-propyl-3H-imidazo[5,1-f]-[1,2,4]-triazin-4-one and HMG-CoA reductase inhibitors, as well as the claimed methods of the invention, would be successful.

As discussed in the previous response (mailed March 5, 2004), the deficiencies of Liao, et al., are not remedied by Niewohner, et al. Niewohner, et al., discloses 2-[2-ethoxy-5-(4-ethyl-piperazine-1-sulfonyl)-phenyl]-5-methyl-7-propyl-3H-imidazo[5,1-f]-[1,2,4]-triazin-4-one; however, Niewohner, et al., does not teach or suggest the combination of 2-[2-ethoxy-5-(4-ethyl-piperazine-1-sulfonyl)-phenyl]-5-methyl-7-propyl-3H-imidazo[5,1-f]-[1,2,4]-triazin-4-one and HMG-CoA reductase inhibitors. Furthermore, based on the disclosure of Niewohner, et al., one skilled in the art would not have been motivated to combine 2-[2-ethoxy-5-(4-ethyl-piperazine-1-sulfonyl)-phenyl]-5-methyl-7-propyl-3H-imidazo[5,1-f]-[1,2,4]-triazin-4-one and HMG-CoA reductase inhibitors to treat sexual dysfunction.

Likewise, neither Doherty, et al., nor R&D Drug News teach or suggest the combination of 2-[2-ethoxy-5-(4-ethyl-piperazine-1-sulfonyl)-phenyl]-5-methyl-7-propyl-3H-imidazo[5,1-f]-[1,2,4]-triazin-4-one and HMG-CoA reductase inhibitors. Both the suggestion and the reasonable expectation of success are lacking.

It is therefore respectfully submitted that Liao, et al., either singly or in combination with Niewohner, et al., Doherty, et al., and R&D Drug Review, fail to teach or suggest the combinations or methods as presently claimed, and that the current invention is novel and nonobvious in view of the prior art references. For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the present rejection.

CONCLUSION

For the foregoing reasons, Applicants submit that the claims are in condition for allowance and Applicants respectfully request reexamination of the present application, reconsideration and withdrawal of the present rejections and objections, and entry of the amendments. Should there be any further matter requiring consideration, Examiner Kim is invited to contact the undersigned counsel.

If there are any further fees due in connection with the filing of the present reply, please charge the fees to undersigned's Deposit Account No. 13-3372. If a fee is required for an extension of time not accounted for, such an extension is requested and the fee should also be charged to undersigned's deposit account.

Respectfully submitted,

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Date: November 19, 2004

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